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(71) Anmelder: Lynx Therapeutics GmbH
69120 Heidelberg (DE)

(72) Erfinder:
, Kramer, Michael Dieter
64319 Pfungstadt (DE)
, Winter, Holger
69120 Heidelberg (DE)
, Reinartz, Jeannette
69121 Heidelberg (DE)

(74) Vertreter:
Rudolph, Ulrike, Dr.
Patentanwältin
In der Schanz 10
69198 Schriesheim (DE)

(54) **mRNA Moleküle zur Verwendung als Indikatoren für den Aktivierungs- und Funktionszustand von T-Lymphozyten**

(57) Die Erfindung betrifft mRNA Moleküle zur Verwendung als Indikatoren für den Aktivierungs- und Funktionszustand von T-Zellen, die dadurch gekennzeichnet sind, daß sie bei aktivierten T-Zellen im Vergleich zum Normal- bzw. Ruhezustand vermehrt oder vermindert exprimiert (auf- bzw. abreguliert) sind und auf dem höheren bzw. niedrigeren Konzentrationsspiegel gehalten werden, und daß sie mit einer der in den Sequenzprotokollen SEQ ID NO. 1 bis NO. 334 dargestellten oder einer davon abgeleiteten oder dazu komplementären Nukleotidsequenz oder einer Teilsequenz davon hybridisieren. Die Erfindung betrifft ferner die in den Sequenzprotokollen dargestellten Nukleotidsequenzen sowie davon abgeleitete oder dazu komplementäre Nukleotidsequenzen oder Teilsequenzen davon (i) zur Verwendung als Nachweisreagenz für den Aktivierungs- und Funktionszustand von T-Zellen, (ii) als bzw. zur Herstellung von Diagnostika und/oder Therapeutika, (iii) zur Identifizierung von medizinisch oder pharmakologisch einsetzbaren Substanzen, (iv) zur Herstellung von Bindemolekülen und (v) zur Herstellung von Testbestecken. Die Erfindung betrifft außerdem die durch die dargestellten Nukleotidsequenzen kodierten Polypeptide, dagegen gerichtete Antikörper und die Verwendung solcher Antikörper zum Nachweis oder zur Beeinflussung des Aktivierungs- und Funktionszustands von T-Zellen.

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New mRNA indicative of T cell activation and functional status, useful for diagnosis and therapy e.g. of autoimmunity or transplant rejection

Patent Assignee: LYNX THERAPEUTICS GMBH (LYNX-N)
Inventor: KRAMER M D; REINARTZ J; WINTER H

Number of Countries: 026 Number of Patents: 002
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Abstract (Basic): DE 10021834 A1

NOVELTY - Messenger RNA, (mRNA), (I), for use as indicator of the activation and functional status of T cells, that have increased or reduced expression, and are present at higher or lower concentration, in activated T cells, relative to normal or resting cells, where (I) hybridizes to any of 334 sequences, reproduced, or their derivatives, complements or fragments, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(a) polynucleotides (II) with any of the 334 specified sequences (or their derivatives, complements or fragments that hybridize to them) for use as reagent for determining the activation or functional status of T cells;

(b) polypeptides (III) derived from (II);

(c) reagent for determining the activation or functional status of T cells comprising (II);

(d) recombinant DNA vector molecules (IV) containing one or more (II) and transcribable in T cells;

(e) antibody (Ab) specific for (III); and (f) binding molecules (IV) that react specifically with (II).

ACTIVITY - Immunosuppressive; immunostimulant; antiinflammatory; cytostatic. No details of tests for any of these activities are given.

MECHANISM OF ACTION - Gene therapy.

USE - Polynucleotides (II) (or their derivatives, complements or sequences that hybridize with them) with any of the 334 specified sequences are used:

(i) as reagent for detecting activation/functional status of T cells, for diagnosis, therapy, modulation or control of the status, in cases of (auto)immunity (against microorganisms, vaccines or allergens); transplant rejection; immunologically-related inflammation; immunosuppression; immune deficiency; guest versus host disease, and malignant diseases of the immune system;

(ii) for identifying agents, potential pharmaceuticals, that bind to (II) or derived polypeptides (III);

(iii) to prepare kits for measuring gene expression profiles in isolated immune, especially T, cells;

(iv) to raise antibodies (Ab) directed against (III); and

(v) to prepare binding molecules (IV) specific for (II).

Ab and (IV) are also useful for detecting and modulating the activation and functional status of T cells.

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Technology Focus:

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preparation: Messenger RNA is isolated from both healthy and diseased tissue, cells or body fluids and, optionally after conversion to cDNA,

Preferred Process: To prepare a test kit for measuring gene expression profiles, mRNA is isolated from both healthy and diseased tissue, cells or body fluids and, optionally after conversion to cDNA, tested for interaction with (II). The mRNA species having different levels of expression in the two cell types are identified. Alternatively;

(i) the isolated mRNAs are tested for binding to immobilized synthetic oligonucleotides (ON) the sequences of which are based on analysis of full-length and/or variant sequences for (II) in different databases; or

(ii) these mRNAs are subjected to polymerase chain reaction (PCR) amplification using primers based on sequences of (II), or on the analysis of (i), and differences in expression of individual genes identified.

Preferred Reagent: In (c), the reagent is:

(i) a polynucleotide labeled e.g. with a luminescence gene; or

(ii) a modified oligo- or poly-nucleotide. Preferred Materials: (IV) are especially antisense RNA molecules, optionally modified, e.g. peptide nucleic acids, and/or ribozymes.